REMARKS

Reconsideration of the application in view of the above amendments and the following remarks is respectfully requested.

Claims 1, 7-9 and 11-12 are pending in the subject application. Claim 1 is the only pending independent claim and the remaining pending claims (7-9 and 11-12) depend directly or indirectly from claim 1. As set forth above, claim 1 has been amended (and thus dependent claims 7-9 and 11-12) to specify that a T cell response is elicited or enhanced by the claimed method. Support for this language is found, for example, at page 10, lines 1-4, of the subject application. No new matter has been added. Therefore, amended claims 1, 7-9 and 11-12 are now pending in the subject application.

As a preliminary matter, the Examiner is thanked for considering the Declaration under 37 C.F.R. § 1.131 filed on April 17, 2002, and in view of the Declaration, removing the previously cited Chatta et al. and Naftzger et al. references as prior art and withdrawing the prior rejections based upon either of these references.

In the Office Action dated June 4, 2002, claims 1, 7, 11 and 12 were rejected under 35 U.S.C. § 103(a) as unpatentable over Disis et al. (J. Immunol. 156:3151-3158, May 1996) in view of any one of Dyrberg et al. (Current Topic in Microbiology and Immunology 130:25-37, 1986), or Mamula (Arthritis and Rheumatism, Vol. 35, suppl., p.S38, 1992), or Fedoseyeva et al. (Transplantation 61:679-683, 1996), or Mahi-Brown et al. (J. Reproductive Immunology 21:29-46, 1992). This rejection is respectfully traversed.

It is respectfully submitted that there was no support, and no showing by the Patent Office, within the legal meaning of Section 103(a) to permissibly combine Disis et al. with another reference in an attempt to establish obviousness. At the time of the subject invention, there was no teaching or suggestion or motivation to combine the teachings of the prior art as attempted by the Office Action. Absent a showing by the Patent Office of a teaching or suggestion or motivation that the combination be made, obviousness cannot be established by such a combination. (*In re Lee*, 277 F.3d 1338, 1343 (Fed Cir. 2002) and cases cited therein.)

It is well established law that, for the purposes of 35 U.S.C. § 103, a reference must be considered as a whole. For example, as recited in *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve*, 796 F.2d 443, 448 (Fed. Cir.1986) (which was quoting from *In re Wesslau*, 353 F.2d 238, 241 (CCPA 1965)):

> It is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one skilled in the art.

Applicants respectfully submit that the Patent Office has not considered Disis et al. as a whole in order to obtain the full appreciation of what this reference fairly suggests to one skilled in the art.

Disis et al. does not merely disclose that overcoming tolerance may be key in the generation of effective anti-tumor immunity, it further discloses a successful approach to overcoming tolerance to a self tumor antigen. Thus, Disis et al., when considered as a whole, would fairly suggest to one of skill in the art that overcoming tolerance to a self tumor antigen may be achieved by use of peptides (of the antigen) from the same species as the individual to be immunized.

More specifically, Disis et al. disclosed that intact rat HER-2/neu protein failed to elicit rat neu-specific immunity in rats. However, rather than attempt to manipulate the conditions of immunization with whole protein, Disis et al. chose to evaluate immunization to peptides (Disis et al. at page 3157, left column, first paragraph). Disis et al. successfully elicited rat neu-specific immunity in rats by immunizing with rat HER-2/neu peptides. Their use of peptides from the same species as was immunized circumvented the tolerance to self protein observed when intact protein from the same species was used. As stated in the abstract (page 3151) of Disis et al.: "These studies suggest an immunization strategy" [the use of human HER-2/neu peptides to immunize humans] "that might be effective in human cancer vaccines targeting self tumor Ag." Disis et al. does not teach or suggest Applicants' immunization strategy or an immunization strategy other than the one that was presented as successful in the reference. Therefore, not only does Disis et al. not provide a teaching or suggestion to combine the cited references as attempted in the Office Action, but due to the success in Disis et al. of overcoming self tolerance (by the use of peptides from the same species as immunized), Disis et al. does not provide motivation for any of the combinations.

When a reference contains its own solution to the problem to which an Applicant's claimed invention is directed, that reference (absent a specific teaching or suggestion in the reference) does not provide a showing under Section 103 that would motivate one of skill in the art to combine that reference with another reference. (*Application of Rinehart*, 531 F.2d 1048, 1054 (CCPA 1976)). Disis et al. contains its own solution (the use of HER-2/neu peptides from the same species to be immunized) to the problem of overcoming tolerance to self tumor antigens. That solution is not employed by Applicants.

Applicants respectfully submit that the Patent Office has failed to particularly point out how Disis et al., when taken as a whole, provides a teaching or suggestion or motivation to combine Disis et al. with another reference. Absent such a teaching or suggestion or motivation, the Patent Office has failed to provide the necessary showing under Section 103 to permit the combining of Disis et al. with another reference. Applicants respectfully submit that for the reasons set forth above, Disis et al. does not provide such a teaching or suggestion or motivation, and accordingly the Patent Office has failed to provide the required showing to permit combining references to assert a rejection under Section 103. Therefore, a *prima facie* case for obviousness has not been established.

Even assuming for the sake of argument that it would be legally permissible to combine Disis et al. with one of the other cited references, it is respectfully submitted that such combinations nevertheless still fail to establish a *prima facie* case for obviousness under Section 103. In the Office Action, Disis et al. is combined with any one of Dyrberg et al.; Mamula; Fedoseyeva et al.; or Mahi-Brown et al. Each of these combinations is addressed in turn.

Disis et al. and Dyrberg et al. is one of the combinations of references for this rejection under Section 103(a). Dyrberg et al. focuses on the initiation of autoimmune responses by foreign pathogens, particularly induction by viruses. Claim 1 (and therefore claims 7-9 and 11-12 which depend therefrom) is directed to a method involving human self tumor antigens. Dyrberg et al. provides no teaching regarding tumor related proteins. At the time of Applicants' invention, there was no reasonable expectation that one of ordinary skill in the art could successfully apply the molecular mimicry of Dyrberg et al. to the human self tumor antigen (HER-2/neu) of Disis et al. or another human self tumor antigen such as PAP.

Another combination is Disis et al. and Mamula for this rejection under Section 103(a). The pending claims are directed to methods involving human self tumor antigens. Mamula discloses the use of cytochrome c to initiate autoimmune responses. Mamula provides no teaching regarding tumor related proteins. At the time of Applicants' invention, there was no reasonable expectation that one of ordinary skill in the art could successfully apply the cytochrome c autoimmunity of Mamula to the human self tumor antigen (HER-2/neu) of Disis et al. or another human self tumor antigen such as PAP.

Another combination is Disis et al. and Fedoseyeva et al. for this rejection under Section 103(a). The pending claims are directed to methods involving human self tumor antigens. Fedoseyeva et al. focuses on elucidating the immune mechanisms underlying long term allograft rejection following transplantation. Fedoseyeva et al. provides no teaching regarding tumor related proteins. At the time of Applicants' invention, there was no reasonable expectation that one of ordinary skill in the art could successfully apply the transplantation teachings of Fedoseyeva et al. to the human self tumor antigen (HER-2/neu) of Disis et al. or another human self tumor antigen such as PAP.

The final combination is Disis et al. and Mahi-Brown et al. for this rejection under Section 103(a). The pending claims are directed to methods involving human self tumor antigens. Mahi-Brown et al. discloses the cellular immune response to immunization with zona pellucida antigens. Mahi-Brown et al. provides no teaching regarding tumor related proteins. At the time of Applicants' invention, there was no reasonable expectation that one of ordinary skill in the art could successfully apply the zona pellucida teachings of Mahi-Brown et al. to the human self tumor antigen (HER-2/neu) of Disis et al. or another human self tumor antigen such as PAP.

Accordingly, Applicants respectfully submit that the Patent Office has failed to establish a *prima facie* case for obviousness of the pending claims under Section 103.

Therefore, it is believed that this rejection of claims 1, 7, 11 and 12 under 35 U.S.C. § 103(a) has been overcome. Withdrawal of this rejection is respectfully requested.

In the Office Action, claims 1, 7-9, 11 and 12 were rejected under 35 U.S.C. § 103(a) as unpatentable over Disis et al. and Dyrberg and Oldstone, and Mamula, and Fedoseyeva et al., and Mahi-Brown et al. as applied to claims 1, 7, 8 11 and 12 in the above

rejection, and further in view of Spitler et al. (U.S. Patent No. 5,925,362). This rejection is respectfully traversed.

It is respectfully submitted that there was no support within the meaning of Section 103 to permissibly combine Disis et al. with Spitler et al. and the other cited references in an attempt to establish obviousness. At the time of the subject invention, there was no teaching or suggestion or motivation in Disis et al. as discussed in detail above to combine the teachings of the prior art as attempted by the Office Action. Absent a teaching or suggestion or motivation that the combination be made, obviousness cannot be established under Section 103 by such a combination. Therefore, the Patent Office has failed to established a *prima facie* case for obviousness under Section 103.

Claim 1 (and therefore claims 7-9 and 11-12 which depend therefrom) recites in part "with an amino acid sequence native to a non-human source." Spitler et al. does not teach or suggest immunizing with an amino acid sequence native to a non-human source. Therefore, Spitler et al. taken alone does not establish a *prima facie* case for obviousness.

As discussed above, there is no basis in the cited art for combining Spitler et al. with any of the other cited references. Even assuming, for the sake of argument, that it would be permissible to combine Spitler et al. with the other cited references, it is respectfully submitted that such a combination fails to establish a *prima facie* case for obviousness. Claim 1 (and therefore claims 7-9 and 11-12 which depend therefrom) is directed to a method involving human self tumor antigens. As described above, none of Dyrberg et al., Mamula, Fedoseyeva et al., or Mahi-Brown et al. provides any teaching regarding tumor related proteins. At the time of Applicants' invention, there was no reasonable expectation that one of ordinary skill in the art could successfully apply the non-tumor related teachings (of Dyrberg et al., Mamula, Fedoseyeva et al., or Mahi-Brown et al.) to the human self tumor antigens of Spitler et al.

Accordingly, Applicants respectfully submit that the Patent Office has failed to establish a *prima facie* case for obviousness of the pending claims.

Therefore, it is believed that this rejection of claims 1, 7-9, 11 and 12 under 35 U.S.C. § 103(a) has been overcome. Withdrawal of this rejection is respectfully requested.

In the Office Action, claims 1, 7, 8, 11 and 12 were rejected under 35 U.S.C. § 102(e) as unpatentable over Carson et al. (U.S. Patent No. 5,679,647). This rejection is respectfully traversed.

As stated in numbered paragraph 7 at page 5 of the Office Action, the method disclosed by Carson et al. involves "administering a polynucleotide". In contrast, pending claim 1 recites, in part, immunizing "with a composition comprising a protein or portion thereof". Administration of a polynucleotide is not the same as with a protein or portion thereof. Accordingly, the pending claims cannot be considered to lack novelty over Carson et al.

Therefore, it is believed that this rejection of claims 1, 7, 8, 11 and 12 under 35 U.S.C. § 102(e) has been overcome. Withdrawal of this rejection is respectfully requested.

Furthermore, not only is the subject matter of pending claims 1, 7-9 and 11-12 not taught by Carson et al., it is not suggested. Carson et al. focuses on the introduction of polynucleotides and the alleged advantages of administering polynucleotides, rather than the direct administration of proteins or peptides. Carson et al. does not teach or suggest that it would be advantageous to substitute proteins (or peptides) for polynucleotides in the immunization process. The reference taken as a whole provides no motivation to substitute proteins (or peptides) for polynucleotides in immunizations.

Carson et al. cites to another Mamula et al. article (J. Immun. 152:1453-1461, 1994), which is now formally made of record by way of the Supplemental Information Disclosure Statement submitted herewith. This Mamula et al. relates to generating B cell and T cell responses against U small nuclear ribonucleoproteins (snRNPs) in order to aid in the understanding of lupus autoimmunity. At pages 1455-1456, Mamula et al. teaches that T cell responses to self snRNPs are elicited by co-immunization with a mixture of foreign snRNPs and self snRNPs (page 1456, left column); however, immunization with foreign snRNPs alone elicits T cell responses to foreign snRNPs but not to self snRNPs (page 1455, left column, last paragraph). As set forth above, amended pending claim 1 (and thus dependent claims 7-9 and 11-12) recites, in part, eliciting or enhancing a T cell response to a human self tumor antigen by immunization with a protein or portion thereof with an amino acid sequence native to a non-human source.... As Mamula et al. teaches that co-immunization (with self snRNPs) is

purportedly required to elicit T cells that recognize this non-tumor self antigen, the subject matter of the now pending claims is neither taught nor suggested.

Further, even assuming that Carson et al. and Mamula et al. (1994) were a permissible combination in accordance with Section 103, the combination still fails to teach or suggest the presently claimed invention.

In the Office Action, claims 1, 7-9, 11 and 12 were rejected under 35 U.S.C. § 103(a) as unpatentable over Carson et al. (U.S. Patent No. 5,679,647) in view of Laus et al. (U.S. Patent No. 6,080,409). This rejection is respectfully traversed.

In numbered paragraph 8 at page 5 of the Office Action, Carson et al. and Laus et al. are characterized. The Office Action then concludes in that paragraph that it would have been *prima facie* obvious "to substitute the polynucleotide encoding prostatic acid phosphate for the polynucleotide encoding prostate-specific transmembrane protein in the method taught by Carson et al.". Even assuming that this substitution was obvious (Applicants do not concede this), the combination still does not yield Applicants' claimed invention. As described above, the pending claims are directed to immunization with proteins (or peptides) and not polynucleotides. As also described above, Carson et al. does not teach or suggest the direct administration of proteins (or peptides).

Accordingly, Applicants respectfully submit that the Patent Office has failed to establish a *prima facie* case for obviousness of the pending claims.

Therefore it is believed that this rejection of claims 1, 7-9 and 11-2 under 35 U.S.C. § 103(a) has been overcome. Withdrawal of this rejection is respectfully requested.

Applicants submit herewith a Supplemental Information Disclosure Statement and a copy of a Mamula et al. (1994) reference disclosed in the cited Carson et al. U.S. Patent. Applicants respectfully submit that the pending claims distinguish patentably over the Mamula et al. reference.

Therefore, in light of the amendments and remarks set forth above, Applicants believe all the Examiner's rejections have been overcome. Reconsideration of the application and allowance of all pending claims (1, 7-9 and 11-12) are respectfully requested. If there is any further matter requiring attention prior to allowance of the subject application, the Examiner is respectfully requested to contact the undersigned attorney (at 206-622-4900) to resolve the matter.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "**Version With Markings to Show Changes Made.**"

Respectfully submitted,
Seed Intellectual Property Law Group PLLC

Richard G. Sharkey, Ph.D.
Registration No. 32,629

Enclosures:

Supplemental Information Disclosure Statement
PTO-1449 (1 sheet)
Mamula et al., J. Immun. 152:1453-1461 (1994)

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Claim 1 has been amended to read as follows:

1. (Thrice Amended) A method of eliciting or enhancing ~~an immune~~ a T cell response to a human self tumor antigen, comprising immunizing a human being with a composition comprising a protein or portion thereof with an amino acid sequence native to a non-human source, wherein the non-human protein or portion thereof has at least 80% amino acid sequence homology to the human self tumor antigen but is not identical in amino acid sequence to the human antigen.